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Tests for Determining the Analgesic Activity Of 1-Phenylisoquinoline Derivatives

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Abstract

In modern medicine, painkillers are widely used in the treatment of diseases and complications of some diseases. According to the World Health Organization, about 30 million people worldwide use painkillers per day. For example, in Malaysia, the consumption of NSAID is 14.2%, of which 4.2% is considered daily consumption. In Iran, it is 14.7% among 35-70-year-olds, and in Saudi Arabia this figure is 14.0%.

Keywords: "Hot plate", "Acetic acid twitching", "Acetylcholine twitching" tests, "twisting" syndrome, pain reflex, analgesic activity.

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1. Introduction

The great need for analgesics with a high level of effectiveness and safe action remains one of the urgent problems of modern medicine. Because currently used analgesics in clinical practice cause a number of side effects, for example, narcotic analgesics cause dependence on the drug, hallucinations, and respiratory depression. Studies have shown that nonsteroidal anti-inflammatory drugs cause a number of side effects in the cardiovascular and gastrointestinal systems [2,3,5].

Therefore, the study of medicinal products obtained from plants containing alkaloids, which do not have the above side effects and have a low toxicity level, is considered a major goal for scientists and researchers.

During our studies, we studied the analgesic activity of 1-phenylisoquinoline derivatives. The fact that the substances under study belong to group IV according to Stefanov's classification, which determines the level of toxicity, has been proven in experiments. The substances under study showed analgesic activity of more than 50% in the "Hot plate" test at doses of 1.0-5.0 mg/kg. In the "Acetic acid twitch" test, the analgesic activity of the substances was found to be more than 60% in the doses of 0.5-5.0 mg/kg. In the "Acetylcholine twitch" test, the analgesic activity of the substances was found to be more than 50% in the doses of 1.0-5.0 mg/kg [1,3,5].

2. Methods

In our studies, the analgesic activity of isoquinoline derivatives was determined by conducting the following tests:

Determination of analgesic activity using the "Hot plate", "Acetic acid twitch" tests:

The "Hot plate" test is used to determine pain sensitivity at the level of central structures of the brain. This test is based on measuring the time it takes for the paws to contact a hot surface until signs of discomfort appear, indicating the occurrence of a pain reflex. The experimental animals were carefully placed on a hot plate heated to 57 0C. The time of onset of discomfort signs was calculated. Each substance was tested on at least 6 mice. 204 white experimental mice weighing 20-22 g were used for the experiment [1,3,5].

The "acetic acid" writhing test is used to assess visceral pain. Pain is induced by intraperitoneal injection of 2.5% acetic acid at a dose of 250.0 mg/kg, which leads to the appearance of the "wriggling" syndrome. The experiment was conducted on 204 white mice weighing 20-22 g. The study substances were administered orally to the animals of the experimental group 60 minutes before the introduction of acetic acid. The number of "wriggling" movements was counted in the experimental and control groups for 20 minutes after the introduction of acetic acid [1,3,5,6].

3. Results and Discussion

In the "hot plate" test, the analgesic activity at doses of 1.0-5.0 mg/kg showed a result of more than 50%. We can see this result in the table below (Table 1).

Table-1.

Analgesic activity of the studied substances in the thermal pain test (hot plate test), M+m, n=6

	Name of groups	Dose mg/kg	The latent period of the pain reaction		
			Normal indicator	After 120 minutes	
			Sonia	Sonia	Increased activity compared to baseline
1	Control physical solution	0.2 ml	9.6±0.8	14.6±0.0	-
2	Ketoprofen	1.0	9.4±0.7	14.2±0.0	51.0
		5.0	9.1±0.4	16.2±0.0	78.0
		10.0	8.8±0.9	**17.2±0.0**	**95.4**
3	1-(2-bromo-4,5-methylenedioxyphenyl)-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline hydrochloride	0.1	9.2±0.5	12.1±0.0	31.5
		0.5	9.5±0.7	12.7±0.0	33.6
		1.0	9.0±0.4	13.2±0.0	46.6
		5.0	8.8±0.8	13.5±0.0	53.4
		10.0	9.5±0.6	14.1±0.0	48.4

Note: *P=0.05 compared to the control group

In the "acetic acid writhing" test, the analgesic activity of the substances at doses of 0.5-5.0 mg/kg was found to be more than 60%. These results are reflected in the table below (Table 2).

Table- 2

Analgesic activity of the studied substances in the chemical pain test (acetic acid writhing test), M+m, n=6

№	Name of groups	Dose mg/kg	The number of folds	% reduction in the number of twitches compared to control.
1	Control Acetic acid 2.5% solution 250.0 mg / kg	0.2	48.4±2.2	-
2	Ketoprofen	1.0	15.2±1.9	68.5
		5.0	**13.8±2.2**	**71.4**
		10.0	16.2±1.8	66.5
3	1-(2-bromo-4,5-methylenedioxyphenyl)-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline hydrochloride	0.1	21.0±2.4	56.6
		0.5	20.6±1.8	57.4
		1.0	17.8±1.6	**63.2**
		5.0	**19.5±2.1**	59.7
		10.0	23.6±2.4	51.2

Note: *P=0.05 compared to the control group of animals

4. Conclusion

The aim of the study was to increase the effectiveness of the use of low-toxic alkaloids obtained from plants in medicine by studying the analgesic effect of isoquinoline derivatives. In conclusion, we can say that the analgesic activity of isoquinoline derivatives was confirmed in experiments by entering them into group IV according to the Stefanov classification, which determines the level of toxicity. The studied substances showed analgesic activity of more than 50% in the "Hot plate" test at doses of 1.0-5.0 mg/kg. In the "Acetic acid writhing" test, the analgesic activity of the substances was found to be more than 60% in doses of 0.5-5.0 mg/kg. In the "acetylcholine twitch" test, the analgesic activity of the substances at doses of 1.0-5.0 mg/kg was found to be more than 50%.

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